A49.E465
JACC March 9, 2010
Volume 55, issue 10A

HYPERTENSION, LIPIDS AND PREVENTION

BEYOND LDL-CHOLESTEROL REDUCTION: EFFECT OF EZETIMIBE IN COMBINATION WITH ATORVASTATIN ON OXIDIZED LDL-CHOLESTEROL IN PATIENTS WITH CORONARY ARTERY DISEASE OR CORONARY ARTERY DISEASE EQUIVALENT

ACC Poster Contributions
Georgia World Congress Center, Hall B5
Sunday, March 14, 2010, 9:30 a.m.-10:30 a.m.

Session Title: Combination Drug Therapy in the Treatment of Hyperlipidemia
Abstract Category: Pharmacology/Hormones/Lipids–Clinical
Presentation Number: 1019-100

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Background: Ezetimibe (eze) is effective in lowering LDL-cholesterol when coadministered with statins. However, the effect of eze on the more atherogenic oxidized LDL cholesterol (ox-LDL) is unknown.

Methods: This is a prospective, randomized, double-blind, placebo controlled trial. Inclusion criteria were stable coronary artery disease (CAD) or CAD equivalent. All patients were placed on atorvastatin (atorva) 40 mg/day and were then randomized to eze 10 mg/day vs. placebo. Patients who were on statin therapy prior to inclusion, were allowed to enter the study as long as the potency of their statin was < atorva 20 mg/day. LDL levels were not entry criteria. Total LDL, LDL particle size, large buoyant LDL, small dense LDL, HDL, VLDL, and ox-LDL, were measured at baseline and following 8 weeks of therapy.

Results: The study population consisted of 100 patients (50 in each group) of whom 90% had stable CAD and 10% had CAD equivalent. Baseline LDL levels were 102 + 29 mg/dL in the eze + atorva 40 mg group and 99 + 21 mg/dL in the placebo + atorva 40 mg group (p = ns). The eze group had larger reduction in total LDL compared to placebo (20% vs. 10% average reduction; p = 0.01). This was mainly due to a larger reduction in large, buoyant LDL (24% vs. 10%; p = 0.008). The reduction in small dense LDL was similar between the 2 groups (32% and 36%; p = ns). Mean LDL particle size increased similarly by 2 angstroms in the 2 groups (p = ns). Ox-LDL was reduced from 51 + 13 U/L at baseline to 46 + 10 U/L at end of therapy in the eze group (p = 0.01) while it did not change in the placebo group (50 + 13 vs. 51 + 13 U/L). Final level of ox-LDL was statistically lower in the eze group compared to the placebo group (p = 0.02). The change in ox-LDL correlated significantly with that of total LDL and of large buoyant LDL (r= 0.6 and 0.5 respectively, p <0.01 for both), but not with that of small dense LDL or HDL or VLDL, indicating that the reduction in ox-LDL was mainly due to a reduction in large buoyant LDL.

Conclusions: Eze decreases mainly large buoyant LDL cholesterol and does not increase LDL particle size. However, it significanlty decreases ox-LDL cholesterol. These findings will be useful in interpretation of on-going clinical trials.